THE VETERINARY JOURNAL

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Vol. 103 May, 1947 No. 5

EDITORIAL

THE CLINICIAN IS IMPORTANT

IF we study the history of the veterinary profession we find that from time to time there have been profound changes in outlook and endeavour. These changes have influenced greatly the line of employment and public relations. This is noticeable particularly if one considers the story of the last 150 years. Those who laid the foundations of the profession were mainly concerned with the welfare of the horse, and rightly so, for the economics of the world at peace or war depended upon that animal.

Other animals were not considered to be of sufficient merit to warrant the attention of the trained and skilled man. The cream of the profession certainly did not bother much about them and they were relegated to those who might be said to be "below the salt." Co-existant with progress in veterinary science, agriculture was also being re-orientated and established as a pursuit more and more dependant upon recognised scientific principles as against the hitherto rule-of-thumb or empirical systems.

As a direct result, attention was focused upon the other animals of the farm until at the present time the bovine species have almost completely displaced the horse from his supreme position. Concurrently, small animal practice has developed in importance.

In the early days the surgeon was of necessity a skilled clinician who had to depend upon his own powers of observation and deduction. His clinical acumen and skill with his hands were his mainstays. In spite of these limitations, a great fount of knowledge was built up. Much of this information was set down and in no mean style, as those who are familiar with the literature of the nineteenth century can testify. Much of this material is as sound to-day as it was when it was written. The surgeons of those days had a profound knowledge of basic drugs, their compounding and action, and by their experimental methods of trial and error they laid the foundations of pharmacology. A successful man had to develop a good memory picture for cases; often his diagnosis was arrived at by this means, for he had seen a similar case before. He had to develop an astute and logical mind, and train his hands and senses.

As the years passed on, the pathologist and bacteriologist came to his aid,

and many new discoveries were made. Some previously established beliefs were confounded, but on the other hand many received scientific confirmation.

Now we have got to the stage when we can also call on such people as radiologists, biochemists, etc. It is possible to get a specialist report on every aspect of a particular case, so that in many instances a diagnosis could be made without seeing the patient—in fact, a policeman could do the job.

No one will deny that it is perfectly correct to make full use of all possible aids to diagnosis, but there are many who think that the pendulum has swung too far and to the detriment of the clinical sense.

It is interesting to note that the same fears assail those in the sister profession.

There is no doubt that the modern young veterinary surgeon has a more complete academic knowledge of the animal body in health or disease, but there is also no doubt that as a clinician he compares unfavourably with his predecessors when the various aids to diagnosis are not forthcoming.

In the pharmacy he is at a disadvantage. In modern times we have learned to depend so much on proprietary drugs, many being of such a complex nature as to be beyond the ordinary individual's comprehension, that we have to take the maker's information for granted. The art of prescribing, compounding and dispensing basic B.P. products is in danger of being lost.

Veterinary medicine must be brought back from the laboratory to the stable and byre. The clinician is the most important man in the profession. If all the laboratories were closed, the profession would live. If the clinicians were removed, the profession would die.

It is to be hoped that when changes in the curriculum and examinations are being considered these points will be borne in mind, and that our teachers will ever remember that veterinary surgeons deal with living animals.

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GENERAL ARTICLES

THE FATE OF CALCIUM AND MAGNESIUM IN THE BLOOD STREAM OF THE RUMINANT

With Special Reference to Treatment of Metabolic Disorders in the Bovine

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Introduction

THE material forming the basis of this paper has been accumulated in two distinct periods, and in each case will be dealt with in the light of the relevant literature available at the time. Certain more recent papers will be discussed in the later sections. The first part of the work was based on normal animals at Weybridge in 1934 and 1935, and was undertaken in connection with the therapeutic use of calcium and magnesium salts in treatment of metabolic disorders of ruminants. The broad lines of approach to this problem were :—

(a) The administration of calcium and/or magnesium by the intravenous, subcutaneous or oral route.

(b) The administration of any glandular extracts which might have the effect of altering the serum magnesium level.

The second part of the work was carried out between 1938 and 1940 on a herd of cows showing seasonal hypomagnesæmia without clinical symptoms (Allcroft and Green, 1938), and was confined to administration of magnesium sulphate by the oral, intravenous and subcutaneous routes.

The correlation of these parts has been held over pending the release of the writer from service in H.M. Forces.

Literature

From the available literature at the start of the experiments, it did not seem likely that oral administration of magnesium salts would materially affect the level of serum magnesium of the ruminant. Barbour and Winter (1931) found that oral administration of magnesium, as the oxide, lactate or gluconate at the rate of 200 mg. per Kg. body weight to dogs caused a rise of serum magnesium of the order 1 mg.p.c. Cunningham (1933) reported large increases in serum magnesium of rats fed very large proportions of magnesium compounds (carbonate, sulphate, phosphate and chloride) in a synthetic diet, but his experiments on sheep and cattle (1934), with relatively smaller doses, were less conclusive. Hirschfelder (1933) found that 20 to 30 g. magnesium sulphate given orally to human subjects produced no change in serum magnesium level unless the subjects were nephritic when marked hypermagnesæmia resulted. Hirschfelder (1934) confirmed his earlier observations on nephritis and reported that administration of magnesium sulphate, in doses from 2 to 10 g. per Kg. to dogs and rabbits, induced hypermagnesæmia of the order 1 to 10 mg.p.c. above the initial level.

The treatment of milk fever and grass tetany is now usually by intravenous administration of calcium and/or magnesium salts. Sjollema and his associates in Holland (Seekles, Sjollema and van der Kaay, 1932) recommended intravenous

injection of 40 g. calcium chloride and 15 g. magnesium chloride in 300 ml. water, basing this on the antagonistic effect of the two mineral ions on the action of the heart. Sjollema (1932), in his review article, gives the outline of this treatment. Greig (1930) reported the successful use of Calcium Sandoz (calcium gluconate) in milk fever. The fate of intravenously injected calcium has been reported by various workers. Hastings and Murray (1921) found an immediate but transient rise in the serum calcium of parathyroidectomised dogs following intravenous injection of 40 ml. of 1 per cent. solution of calcium chloride. Whelan (1925) studied the effect of slow intravenous chloride injections in man and dogs: if the injection was slow enough, there was no rise in blood chloride, though urinary chloride rose immediately. Calcium and magnesium showed an instant rise, but had returned to normal in four or five hours, while sodium and potassium only remained high for about 30 minutes. Taylor and Fine (1930) found that calcium injected intravenously into animals left the blood stream, but not the body, in three hours. Liebermann (1930) found that the maximum safe dosage of calcium by the intravenous route was of the order 35 to 40 mg. per Kg. in dogs. Greville (1931), using etherised rabbits, found that at any time greater than five minutes after the intravenous injection of calcium, as chloride or lævulinate, the rate of fall of serum calcium was proportional to the excess at that time over the final constant level.

Studies have also appeared on the subcutaneous injection of various salts. Neuwirth and Wallace (1929) injected magnesium sulphate into dogs at two different levels: at 0.25 g. per Kg. serum magnesium rose from 2.4 to 5.3 mg.p.c. in one hour and stayed at about 4.8 mg.p.c. for a further five hours, but was normal again after 24 hours; at 2.7 g. per Kg., the serum magnesium rose to 19.8 mg.p.c. in 50 minutes and to 20.3 mg.p.c. in a further 30 minutes. Brookfield (1934) reported that subcutaneous injection of either calcium or magnesium in rabbits raised the level of the mineral injected and lowered that of the other. Weston and Howard (1923) showed that magnesium sulphate was tolerated even in 50 per cent. solution intramuscularly in human mental patients.

The level of serum magnesium is known to affect the response to nervous stimuli. Hirschfelder (1933) noted that coma was induced when the serum magnesium level was around 17 mg.p.c., while Neuwirth and Wallace (1932) had observed relaxation and depression in dogs when the serum magnesium level was raised to 5 or 6 mg.p.c. The possible relation of endocrine glands to the serum magnesium level has received some attention. Cannavò and his associates have reported association between the pituitary gland and the level of serum magnesium. Cannavò (1932) and Cannavò and Indovina (1932) reported that subcutaneous injections of large doses of "Prolan" for 10 days in man, rabbits and dogs resulted in marked hypermagnesæmia, which persisted for 15 days after the last injection; serum calcium was not affected. Schulhof (1933) found that massive doses of "Prolan" in sheep did not alter serum magnesium. Hoffman and Anselmino (1934) found that massive doses of "Prolan" injected into dogs and rats raised serum calcium but did not affect serum magnesium. Cannavò and Beninato (1934) showed that X-ray destruction of the pituitary of rabbits led to a sharp fall in serum magnesium, which remained low till death supervened in 15 to 20 days. Dell 'Acqua (1935) found that "Prolan" injections in cats raised

serum magnesium and did not alter serum calcium, and further stated that neither adrenal cortex hormone nor insulin had any effect on serum calcium or magnesium. In assessing the work of Cannavò and his associates, the writer is handicapped by not having seen the originals and in being uncertain of the product injected, as the titles refer to " Prolan " or anterior pituitary hormone. The short survival period, 15 to 20 days, after X-ray destruction of the pituitary (Cannavò and Beninato, 1934) suggests that parts of the brain might have been damaged and the changes in serum magnesium might not be due solely to the ablation of the pituitary.

Cahane (1928) found no change in the calcium or magnesium content of the muscle of cats, dogs, guinea pigs or rats following fresh thyroid treatment. Weaver and Reed (1930) reported that complete thyroparathyroidectomy in the dog lowered serum calcium but had no effect on serum magnesium. Scholtz (1931) and Greenberg and Mackey (1932) noted that following injection of parathyroid extract there was a small transient rise in serum magnesium, which regained its normal level before the maximum rise of serum calcium had taken place. Bulger and Gausmann (1933) found that clinical cases of hyperparathyroidism were in negative magnesium balance, but showed normal serum magnesium levels.

Results of Experiments on Normal Cattle and Goats, 1934 and 1935. Anæsthetic and Lethal Levels of Serum Magnesium.

Pilot experiments to determine the anæsthetic and lethal levels of serum magnesium were undertaken on goats. Representative sets of data for these series of experiments are given.

In the first series, a 50 per cent. solution of magnesium sulphate was used and the dose was graduated at 1.875 g. magnesium sulphate per Kg. body weight. One-third of the dose was given by the intravenous route and the remainder subcutaneously. This meant that the 20 Kg. goat used in the experiment recorded in Table I and Fig. 1 received 25 ml. intravenously and 50 ml. subcutaneously.

TABLE I

RESULTS OF INDUCING MAGNESIUM ANÆSTHESIA IN A GOAT OF 20 KILO BY INJECTION OF 25 c.c. 50 PER CENT. MAGNESIUM SULPHATE INTRAVENOUSLY AND A FURTHER 50 c.c. SUBCUTANEOUSLY.

Dates and Timings of Samples.	Blood Constituents: mg. p.c. Serum Calcium	Serum Magnesium	Blood Sugar
7 January, '35	9.8	2.6	56
8 „ '35	9.9	2.5	62
9 „ '35	9.9	2.5	64
10 „ '35 before injection	9.8	2.4	64
5 mins. after injection ...	9.4	12.2	68
1 hour „ „ ...	8.7	10.7	82
2 hours „ „ ...	8.6	9.9	97
4 „ „ „ ...	8.7	7.9	105
6 „ „ „ ...	8.6	7.4	101
11 „ '35	8.6	2.9	63
12 „ '35	8.6	2.3	64

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In these experiments a light anæsthesia was produced for a period of 5 to 10 minutes, and coincided with levels of serum magnesium around 12 mg.p.c. There were no ill-effects from these injections. In addition to the elevation of magnesium, it was found that there was depression of the calcium level, which was between 10 and 15 per cent. lower an hour after injection and stayed low for periods varying from 6 to 48 hours. The blood sugar showed a rise which was

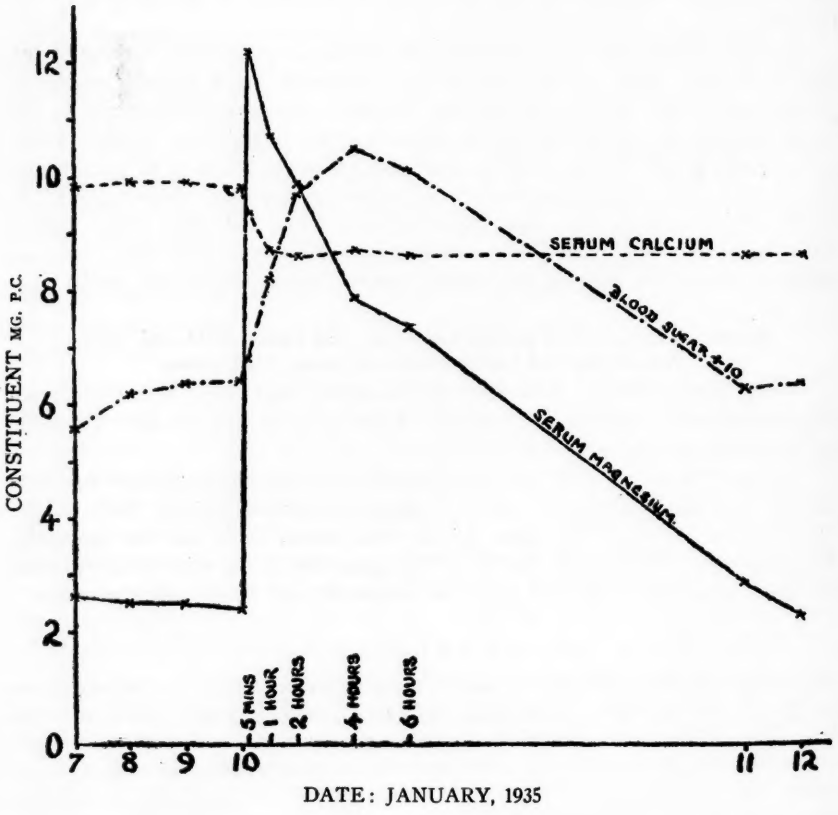

FIG. 1.
Behaviour of blood constituents of a goat after intravenous injection of magnesium sulphate: 1.875 g. per Kg. body weight.

not as rapid as the rise in serum magnesium, but the high level persisted for several hours after the peak of the serum magnesium curve; the order of elevation of blood sugar was 55 to 75 per cent. of the initial level.

In the next series of experiments a 50 per cent. solution of magnesium sulphate was injected subcutaneously at the rate of 3 g. per Kg. body weight. The results are illustrated in Table II, where a goat of 25 Kg. was used.

TABLE II

RESULTS OF INDUCING MAGNESIUM ANÆSTHESIA IN A GOAT OF 25 KILO BY INJECTION OF MAGNESIUM SULPHATE SUBCUTANEOUSLY AT THE RATE OF 3 GRAMS PER KILO.

Dates and Timings of Samples.	Blood Constituents: mg. p.c. Serum Calcium	Serum Magnesium	Blood Sugar
28 January, '35	8.6	2.2	56
29 „ '35 before injection	8.4	2.1	56
5 mins. after injection ...	8.3	11.6	69
1 hour „ „ ...	7.1	12.8	163
2 hours „ „ ...	7.0	13.7	187
4 „ „ „ ...	6.2	14.0	184
6 „ „ „ ...	7.3	14.4	185

In these experiments anæsthesia was induced about the fourth hour after injection, when the serum magnesium level was between 13.5 and 14.5 mg.p.c., and the animals remained comatose and indifferent to external stimuli until death supervened some seven to nine hours after injection. The blood sugar showed a sharp rise in the first hour and remained elevated at about 180 mg.p.c. for the period of survival. These findings on blood sugar confirmed the earlier work of Kleiner and Meltzer (1916) and of Ogawa (1936). The serum calcium showed a fall of 25 per cent. in the first four hours and a tendency to rise again in the later samples. Blood samples were not obtained from any of these animals within two hours of death.

To determine the lethal level of serum magnesium, two goats of 30 Kg. were used. The first received 90 g. magnesium sulphate intravenously and died in less than an hour without regaining consciousness. The second was given the same dose subcutaneously and died in seven hours. These experiments are recorded in Table III.

TABLE III

RESULTS OF INJECTING 90 g. MAGNESIUM SULPHATE (*a*) INTRAVENOUSLY, AND (*b*) SUBCUTANEOUSLY IN GOATS.

Time Relative To Injection	Blood Constituents: mg. p.c. Goat 7: Intravenous Serum Calcium	Serum Magnesium	Blood Sugar	Goat 10: Subcutaneous Serum Calcium	Serum Magnesium	Blood Sugar
Before	8.5	2.2	61	... 9.0	2.1	47
15 mins. after	8.0	20.5	201	... 9.0	12.7	69
1 hour „				... 7.5	13.9	117
2 hours „				... 6.5	16.3	154
4 „ „				... 7.0	19.0	150
6 „ „				... 8.0	20.7	122

As the serum magnesium levels of both goats just about the time of death were about 20 mg.p.c., it would appear that this is the lethal level for the goat. The blood sugar of the first goat rose very rapidly, while that of the second goat, subcutaneously injected, rose more slowly, to a lesser degree, and was falling again prior to death. The serum calcium of the second goat showed a 27 per cent.

decrease in the first two hours, followed by a tendency to return to normal (see also the results in Table II).

In order to see if the hyperglycæmia was due to anæsthesia, a series of goats were anæsthetised with Evipan Sodium, administered intravenously. The results of two of these experiments are shown in Table IV.

TABLE IV

RESULTS OF EVIPAN ANÆSTHESIA IN TWO GOATS.

Time Relative To Injection	Blood Constituents: mg. p.c. Goat A Serum Calcium	Goat A Serum Magnesium	Goat A Blood Sugar	Goat B Serum Calcium	Goat B Serum Magnesium	Goat B Blood Sugar
Before	8.8	2.7	63	8.5	2.3	63
5 mins. after	8.8	2.7	62	8.1	2.3	62
2 hours „	8.3	2.8	65	8.5	2.5	63
4 „ „	8.9	2.9	74	8.5	2.4	65
6 „ „	9.1	2.7	63	8.9	2.5	68
24 „ „	8.8	2.7	56	8.9	2.4	59

In neither case was any significant change in serum calcium, serum magnesium or blood sugar noted. To see if hyperglycæmia had any effect on the level of serum magnesium, some goats were injected with adrenalin hydrochloride at the rate of 0.5 mg. per Kg. body weight. Table V shows the results of a typical series of analyses.

TABLE V

RESULTS OF INJECTION OF ADRENALIN AT THE RATE OF 0.5 mg. PER KILO IN A GOAT.

Time Relative To Injection	Blood Data: mg. p.c. Serum Calcium	Serum Magnesium	Blood Sugar	Blood Inorganic P	Red Cell Volume %
Before	8.5	2.4	51	4.8	38
5 mins. after	8.1	2.5	102	5.2	50
15 „ „	8.2	2.6	144	5.3	42
30 „ „	7.8	2.5	166	5.5	38
90 „ „	8.2	2.4	149	5.3	35
2 hours „	8.5	2.4	141	5.1	38
3 „ „	7.8	2.5	105	5.0	37
4 „ „	8.4	2.5	94	4.8	38
5 „ „	8.4	2.5	91	4.4	38
24 „ „	8.3	2.2	57	4.7	37

The elevation of blood sugar by injection of adrenalin was not accompanied by any significant alteration of the levels of serum calcium or serum magnesium, but there was a small rise in inorganic phosphorus, the curve of which runs roughly parallel to that for blood sugar, and a temporary increase in the volume of red blood cells, which was normal again half an hour after injection.

Experiments in Connection with Therapeutic Treatments for Metabolic Disorders

The experiments in this connection were carried out on normal cattle, either males or females, of approximately 1,000 lb. live weight, and the results are therefore comparable at sight.

Intravenous Injections

A standard procedure for all intravenous injection experiments, on goats

or cattle, was followed throughout. The pre-injection sample was taken by means of a hypodermic needle inserted into the left jugular vein, which was raised by partial stasis, and the solution was injected *via* that needle without removing it from the vein. All subsequent samples for that experiment were taken from the right jugular vein, in order to avoid possible contamination from any drops of the injected solution which might remain on the hide or coat of the animal. The first sample of blood was taken five minutes after injection, and others at suitable intervals. Sjollema's therapeutic injection for milk fever and grass tetany was first tried. This involves intravenous injection of 300 ml. of solution containing 40 g. calcium chloride and 15 g. magnesium chloride, the quantities of mineral elements injected being 7.33 g. Ca and 1.8 g. Mg. Table VI and Fig. 2 show the results of one of this series of experiments.

TABLE VI

RESULTS OF INTRAVENOUS INJECTION OF SJOLLEMA'S TREATMENT (40 GRAMS CALCIUM CHLORIDE AND 15 GRAMS MAGNESIUM CHLORIDE IN 300 C.C. WATER)

Time Relative To Injection	Serum Calcium mg. p.c.	Serum Magnesium mg. p.c.
Before	10.0	2.2
5 mins. after	22.5	5.1
30 „ „	16.2	3.9
90 „ „	13.2	2.9
3 hours „	10.8	2.3
6 „ „	10.2	2.2
12 „ „	10.2	2.2
24 „ „	9.7	2.3
48 „ „	10.0	2.2

The increase in both calcium and magnesium was of the order 125 to 150 per cent. and they both show similar percentage rates of decline till the initial levels were regained between the third and sixth hour after injection.

The separate injection of the calcium and magnesium equivalents of the Sjollema injection were made in a further series of experiments, using 825 ml. of 10 per cent. Calcium Sandoz and 100 ml. of 18 per cent. magnesium sulphate respectively. Representative experiments are recorded in Table VII and Fig. 3.

TABLE VII

RESULTS OF SEPARATE INJECTIONS OF THE CALCIUM AND MAGNESIUM EQUIVALENTS OF THOSE USED IN THE SJOLLEMA INJECTION (TABLE VI).

Time Relative To Injection	Serum Data: mg. p.c. 7.33 g. Ca. Calcium	Magnesium	1.8 g. Mg. Calcium	Magnesium
Before	9.8	2.0	10.2	1.9
5 mins. after	25.1	2.0	10.2	6.2
30 „ „	18.0	2.0	10.1	3.8
90 „ „	13.9	1.8	10.6	2.8
3 hours „	11.6	1.8	10.4	2.3
6 „ „	10.3	1.9	10.6	1.8
12 „ „	9.6	2.1	10.6	1.8
24 „ „	10.0	2.1	10.7	1.9
48 „ „	10.1	2.1	10.6	1.9

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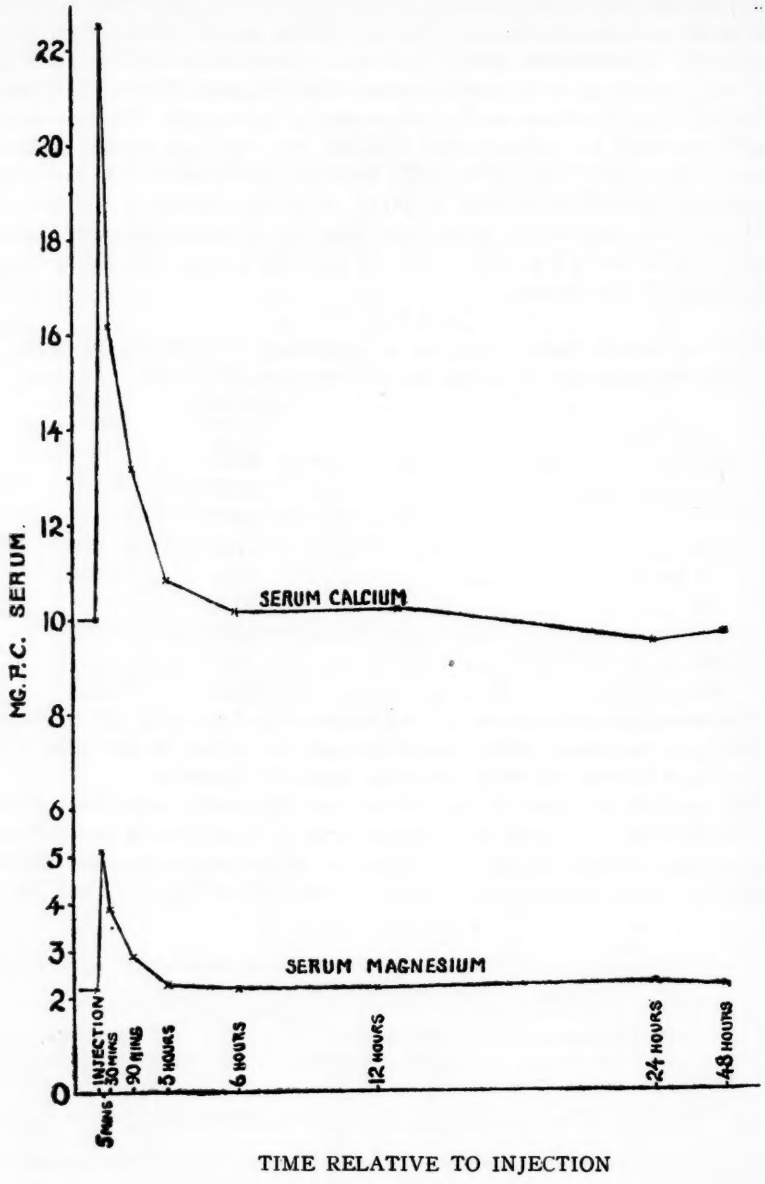

FIG. 2.
Behaviour of blood constituents after intravenous injection of Sjollema's recommended therapy: 40 g. calcium chloride and 15 g. magnesium chloride (equivalent to 7.33 g. Ca and 1.8 g. Mg) in a 1,000 lb. bovine.

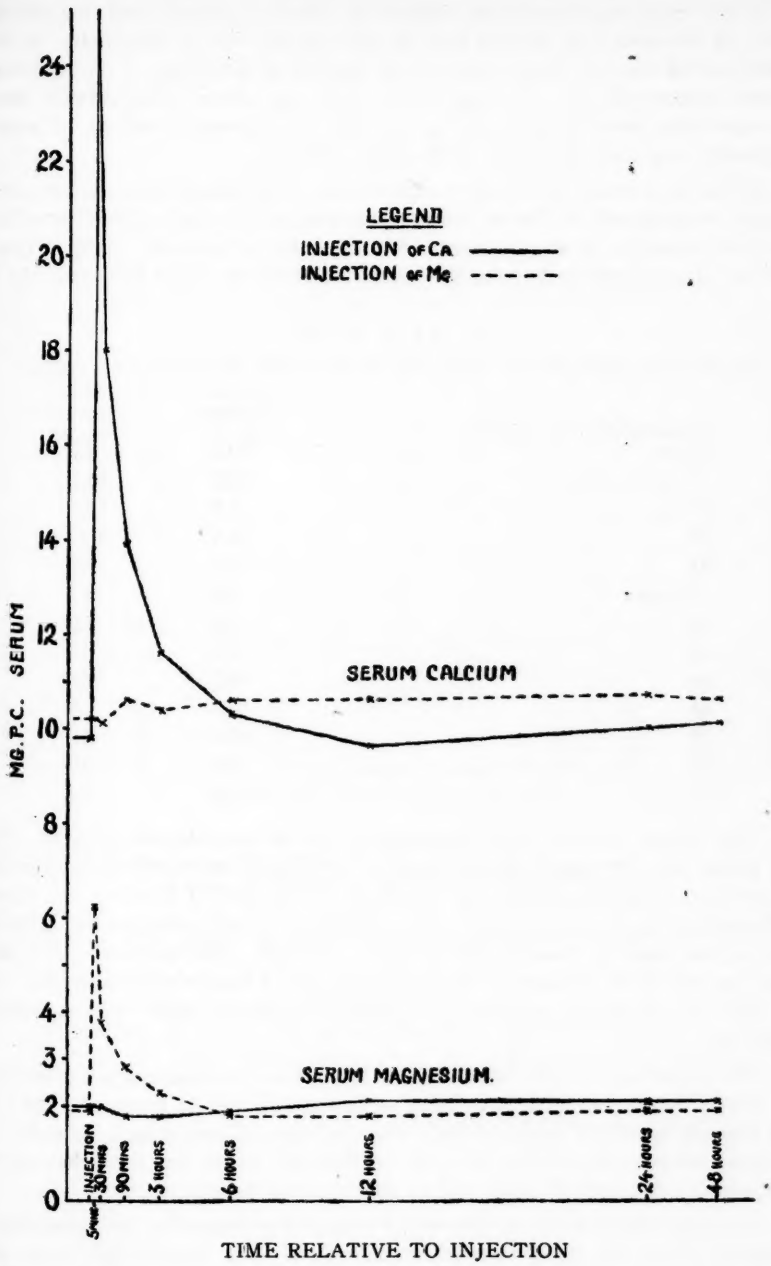

FIG. 3.

Behaviour of blood constituents after intravenous injection of calcium gluconate equivalent to 7.33 g. Ca, in a 1,000 lb. bovine.

From these experiments the individual elements, calcium and magnesium, behave in the same way whether they are injected together or separately. At the concentrations used for these experiments there is no indication of the reciprocal relation between calcium and magnesium, which was shown when massive doses of magnesium were injected into goats, with consequent elevations of serum magnesium and some lowering of the serum calcium.

In the next series of injection experiments, 75 g. magnesium sulphate were injected intravenously in 300 ml. water, since this was the type of injection which was being employed in the treatment of grass tetany or lactation tetany in Great Britain. Representative data for this series are shown in Table VIII and Fig. 4.

TABLE VIII

RESULTS OF INTRAVENOUS INJECTION OF 75 GRAMS MAGNESIUM SULPHATE.

Time Relative To Injection	Serum Calcium mg. p.c.	Serum Magnesium mg. p.c.
Before	10.8 ...	2.2
5 mins. after	10.0 ...	14.5
10 „ „	8.8 ...	12.3
30 „ „	9.5 ...	10.3
90 „ „	9.9 ...	6.2
3 hours „	9.8 ...	4.3
6 „ „	9.9 ...	3.0
12 „ „	11.0 ...	2.8
24 „ „	10.2 ...	2.3
48 „ „	10.2 ...	1.9
72 „ „	...10.4 ...	2.0
96 „ „	8.8 ...	2.2
120 „ „	10.0 ...	2.1

The clinical side of these experiments was of considerable interest. The respiration rate decreased and the depth of respiration increased as the injection proceeded, and as the needle was withdrawn at the end of injection the animal collapsed in a semi-comatose state. The samples taken five minutes after injection were drawn from the animals still recumbent and dull. The animals rose of their own free will 10 to 12 minutes after injection, and a sample was taken then. At no time was there any evidence of cardiac irregularity, other than a reduced heart rate.

Five minutes after the injections, the level of serum magnesium was between 14 and 15 mg.p.c., and this had fallen to between 12 and 13 mg.p.c. by the time the animals stood up again of their own volition. There was a reduction of calcium, between 18 and 23 per cent. in different cases, but the behaviour of calcium was not strictly reciprocal to that of magnesium.

Dryerre (1932) proposed the use of magnesium lactate for the treatment of lactation tetany, his solution being composed of 33 g. magnesium lactate and 8 c.c. syrupy phosphoric acid in 1,000 ml., to which he added 25 g. Na_2HPO_4 dissolved in 120 ml. water. This volume of solution, 1,120 ml., took 10 minutes to inject by gravity, and the first sample was taken 30 minutes after the start

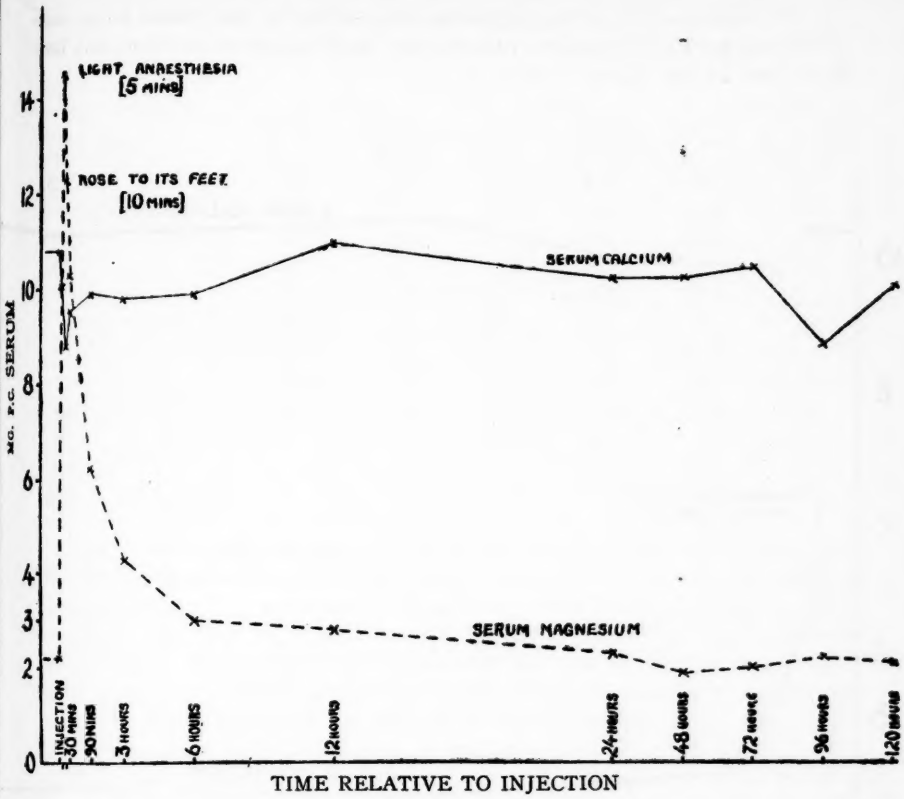

FIG. 4.
Behaviour of blood constituents after intravenous injection of magnesium sulphate, equivalent to 1.8 g. Mg. in a 1,000 lb. bovine.

of injection. The results of one trial of this injection are given in Table IX and Fig. 5.

TABLE IX

RESULTS OF INJECTION OF DRYERRE'S THERAPEUTIC SOLUTION (CONTAINING 33 g. MAGNESIUM LACTATE IN 1,120 c.c.) INTRAVENOUSLY.

Time Relative To Injection	Serum Calcium mg. p.c.	Serum Magnesium mg. p.c.
Before	10.4	1.8
30 mins. after	10.4	4.5
90 „ „	9.8	3.2
3 hours „	9.9	2.2
6 „ „	9.9	2.0
12 „ „	10.6	1.8
24 „ „	10.3	1.8
48 „ „	10.5	1.8

The behaviour of serum magnesium was similar to that shown when comparable amounts of magnesium were injected as the sulphate and there was little disturbance of the calcium level.

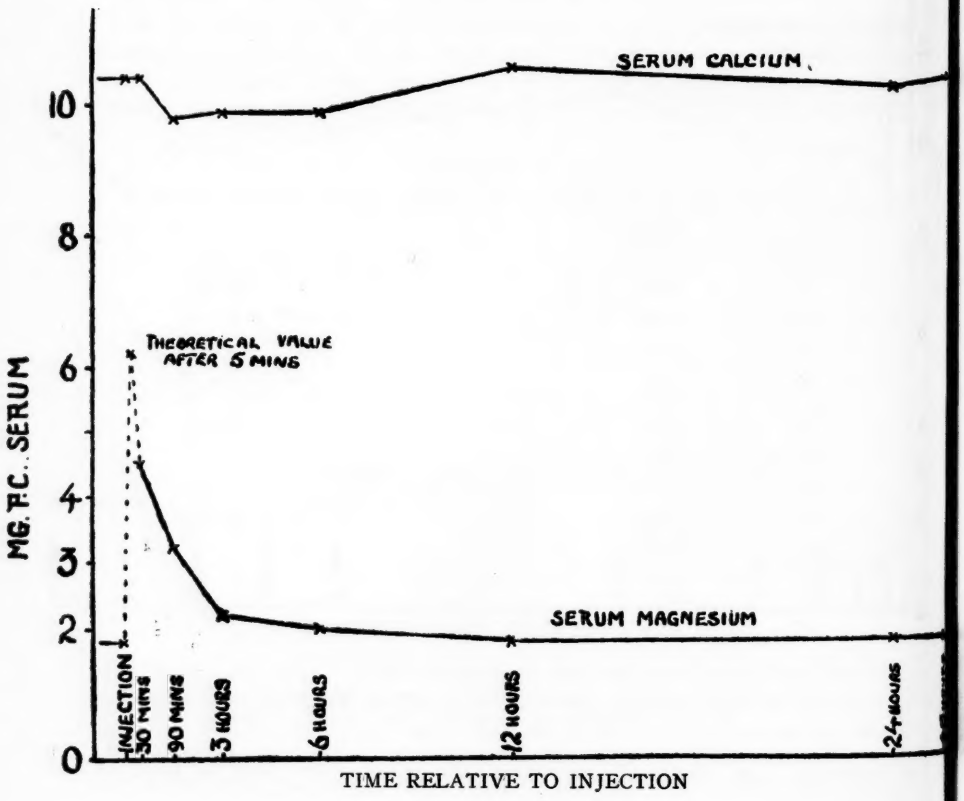

FIG. 5.
Behaviour of blood constituents after intravenous injection of Dryerre's therapy (33 g. magnesium lactate) in a 1,000 lb. bovine.

Subcutaneous Injections

Magnesium sulphate was injected subcutaneously at three different levels: 25 g., a quantity which had been used therapeutically by a number of veterinary surgeons with varying reports on its value; 75 g., to compare with the same quantity injected intravenously (Table VIII); and 115 g., approximately 4 oz., as recommended by this Laboratory for use in cases of lactation tetany. Data for these three levels are given in Table X, and, as there were no changes in serum calcium in any of the experiments, the serum magnesium curves only are given in Fig. 6.

TABLE X

RESULTS OF SUBCUTANEOUS INJECTIONS OF MAGNESIUM SULPHATE AT DIFFERENT RATES.

Time Relative To Injection	25 grams Serum Calcium mg. p.c.	25 grams Serum Magnesium mg. p.c.	75 grams Serum Calcium mg. p.c.	75 grams Serum Magnesium mg. p.c.	115 grams Serum Calcium mg. p.c.	115 grams Serum Magnesium mg. p.c.
Before	10.1	1.8	9.5	1.9	10.5	2.2
5 mins. after ...	10.1	1.8	9.4	2.0	10.5	2.6
30 „ „ ...	10.1	2.6	9.4	3.8	10.3	4.2
90 „ „ ...	10.1	2.7	9.2	4.4	10.3	5.0
3 hours „ ...	10.0	2.9	10.0	4.3	10.3	5.2
6 „ „ ...	10.3	2.6	9.7	3.6	10.3	5.0
12 „ „ ...	10.3	2.2	8.7	2.6	10.5	4.1
24 „ „ ...	10.2	1.9	8.7	2.0	10.4	2.6
48 „ „ ...	10.1	1.9	9.6	1.9	9.0	2.1
72 „ „ ...			9.5	2.0	9.3	2.1
96 „ „ ...					10.4	2.0
120 „ „ ...					10.5	2.1

25 g. magnesium sulphate induced a rise of 0.8 mg.p.c. which lasted from the first to the sixth hour after injection. 75 g. magnesium sulphate raised the serum magnesium by 1.9 mg.p.c. (100 per cent.) after 30 minutes, and the highest recorded value was 4.4 mg.p.c. after 90 minutes. Hypermagnesæmia persisted for 12 hours. 115 g. magnesium sulphate raised the maximum level to 5.2 mg.p.c. three hours after injection; even after 12 hours the level was almost 100 per cent. above the initial figure and was still up 24 hours after injection.

Experiments with a suspension of magnesium lactate, either in water or in a 10 per cent. solution of magnesium sulphate, were made to see if the period of elevation of serum magnesium could be prolonged. It was found that there was no advantage from using this compound and that the procedure led to stiffness and swelling at the site of injection. No figures or curves for these experiments are included.

Subcutaneous injection of calcium was only tried in one series of experiments, in which 825 ml. calcium gluconate (see Table VII) was used. Data are given in Table XI.

TABLE XI

RESULTS OF SUBCUTANEOUS INJECTION OF 825 c.c. 10 PER CENT. CALCIUM SANDOZ (7.33 g. Ca.)

Time Relative To Injection	Serum Calcium mg. p.c.	Serum Magnesium mg. p.c.
Before	9.7 ...	2.0
5 mins. after	9.9 ...	2.0
30 „ „	10.7 ...	2.0
90 „ „	11.6 ...	1.9
3 hours „	11.6 ...	2.0
6 „ „	11.1 ...	1.9
12 „ „	10.8 ...	2.0
24 „ „	9.8 ...	2.0

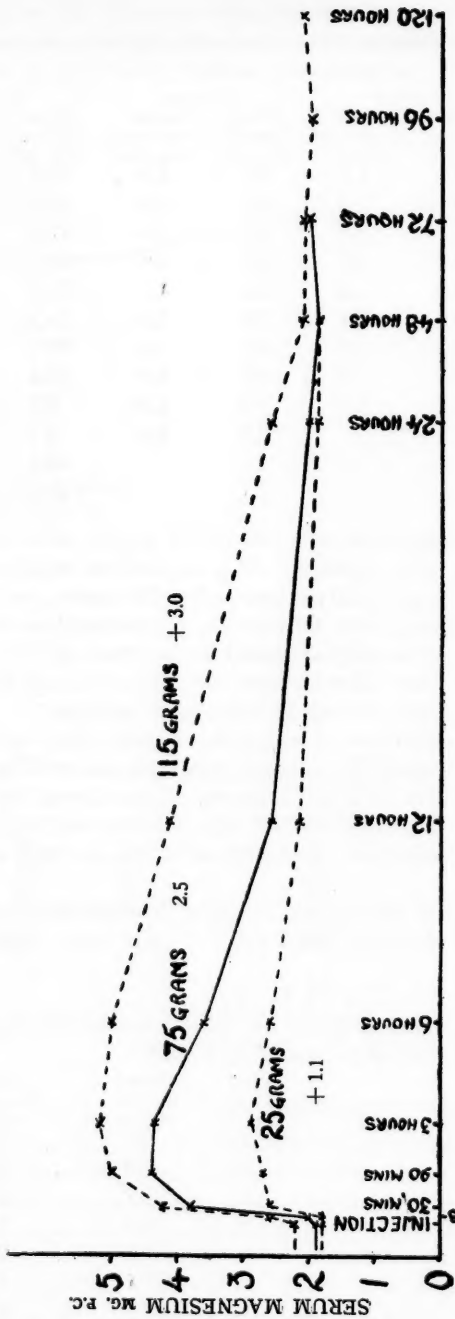

FIG. 6.
Behaviour of serum magnesium after subcutaneous injections of magnesium sulphate at three different levels in a 1,000 lb. bovine.

This procedure resulted in elevation of the serum calcium by about 2 mg.p.c. over the period from 90 minutes to 3 hours after injection, and produced no effect on serum magnesium level.

Injections of "Prolan" Subcutaneously in Rabbits, Goats and Heifers

Daily injections of 125 rat units of Prolan for 10 days in rabbits had no effect on the calcium or magnesium level of the serum.

Injections of either 125 or 250 rat units into goats also had no effect on either serum calcium or magnesium. Injections of 125 or 1,250 rat units into heifers produced no significant alteration in serum magnesium level, but did cause a temporary slight hypercalcæmia.

It is not considered necessary to include the data of these experiments in this paper in view of the negative findings.

Oral Dosage of Magnesium Sulphate

A single oral drench of 200 g. magnesium sulphate made no difference in the level of serum magnesium in periodic samples up to 24 hours after dosing.

Daily oral dosage of 90 g. magnesium sulphate for seven days failed to effect any change in the serum magnesium level.

Discussion of Results of Experiments on Normal Animals

Oral dosage of magnesium sulphate and subcutaneous injections of "Prolan" were ineffective in altering the level of serum magnesium.

Intravenous injections of calcium and/or magnesium salts resulted in immediate increase in the level of the mineral or minerals injected, the rise depending on the amount injected. Thereafter the disappearance of excess calcium and/or magnesium followed very closely the principles postulated by Greville (1931). In intravenous therapy there is a limit to the amount of either calcium or magnesium which can be safely administered. Assuming that the upper limit of 35 to 40 mg. calcium per Kg., found by Liebermann (1930) in the dog, is applicable to cattle, the safe intravenous dose for 1,000 lb. cow would be 18.2 g. calcium, equivalent to about 100 g. calcium chloride or 210 g. calcium gluconate. From experiments reported above, it would appear that 75 g. magnesium sulphate is about the maximum quantity which is safe to inject intravenously into a 1,000 lb. cow; this dosage is approximately 16.5 mgs. magnesium per Kg. body weight.

Comparison of the intravenous and subcutaneous routes of administration shows that for the same amount injected the former results in greater elevation of shorter duration, while the latter produces a smaller increase but maintains an elevated serum level for a longer time. On theoretical grounds, it would therefore appear better to give injections subcutaneously unless it is imperative to effect an immediate elevation of the calcium or magnesium level of the serum. The injection of calcium borogluconate (Hayden, 1934) is now the usual treatment for milk fever cases, and it can be given either intravenously or subcutaneously with little risk, though Morgan and Morgan (1945) have advocated the inclusion of carbolic acid in the solution and the massage of the site of injection to avoid the risk of abscess formation. The majority of practitioners favour the intravenous route, and as it is urgent to correct this hypocalcæmia, this would appear

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sound as a first action and might well be followed by subcutaneous injection of further calcium in the event of being called in to treat a case that has relapsed after temporary recovery.

In treatment of lactation tetany cases, most of which show hypocalcæmia and hypomagnesæmia, there is the additional factor of hyperexcitability to be considered when advising on treatment. Magnesium sulphate is cheap, readily available and can safely be used in concentrations up to 50 per cent. by the subcutaneous route, but it cannot be used in the same solution as a calcium compound owing to precipitation of calcium sulphate, and its use in cases where both calcium and magnesium injections are indicated involves the use of two solutions. This factor is really no disadvantage as the employment of separate solutions of calcium and magnesium allows treatment to be varied to suit the clinical indications and also allows of the use of magnesium first to quieten the animal.

It is considered advisable to stress the question of the temperature of the fluid to be injected. Whether the injection was intravenous or subcutaneous, the solution was always injected within 2 degrees of body temperature and no abscess formation ever occurred. The injection of solutions too hot or too cold is liable to result in local tissue damage and even abscess formation.

Results of Administration of Magnesium Salts to Hypomagnesæmic Cattle, 1938 to 1940

In connection with extension of the work on seasonal hypomagnesæmia of the bovine without clinical symptoms (Allcroft and Green, 1938), several experiments were carried out on animals of the herd of Hereford cows at Swanton Farm. It is stressed that these animals, even when showing serum magnesium values as low as 0.5 mg.p.c., were apparently normal, healthy cattle, and that rounding them up on horseback and yarding them for bleeding did not produce any more evidence of excitement in winter than in summer, when the magnesium level of the serum was normal.

In January, 1938, four cows, whose serum magnesium values varied from 1.5 to 1.9 mg.p.c., were used. Two received 1 ounce of magnesium sulphate intravenously, and the other two received 3 ounces subcutaneously. The data are given in Table XII and the serum magnesium curves in Fig. 7.

TABLE XII

RESULTS OF INJECTIONS OF MAGNESIUM SULPHATE INTO COWS WITH SEASONAL HYPOMAGNESÆMIA WITHOUT CLINICAL SYMPTOMS—JANUARY, 1938

	1 oz. intravenously				3 oz. subcutaneously			
	Cow A		Cow B		Cow C		Cow D	
Time relative to injection	Serum Calcium mg.p.c.	Serum Magnesium mg.p.c.	Serum Calcium mg.p.c	Serum Magnesium mg.p.c.	Serum Calcium mg.p.c.	Serum Magnesium mg.p.c.	Serum Calcium mg.p.c.	Serum Magnesium mg.p.c.
Before	9.8	1.9	10.1	1.6	... 9.4	1.9	9.7	1.5
5 mins. after...	9.9	6.6	10.0	6.4	... —	—	—	—
30 „ „ ...	9.8	5.1	10.1	4.8	... 9.4	2.9	9.8	2.5
90 „ „ ...	10.0	3.3	9.9	3.1	... 9.4	4.1	9.9	3.8
3 hours „ ...	9.8	2.9	10.1	2.8	... 9.6	4.3	9.8	4.1
6 „ „ ...	10.1	2.2	10.0	2.0	... 9.3	3.3	10.1	3.5
24 „ „ ...	10.0	2.0	10.0	1.7	... 9.5	1.8	9.8	1.6

SERUM MAGNESIUM MG. P.C.

XUM

In both series of injections the serum magnesium returned to approximately the initial level in 24 hours and, in the case of cows B and D, did not steady at a normal value for the average cow, around 2 to 2.5 mg.p.c.

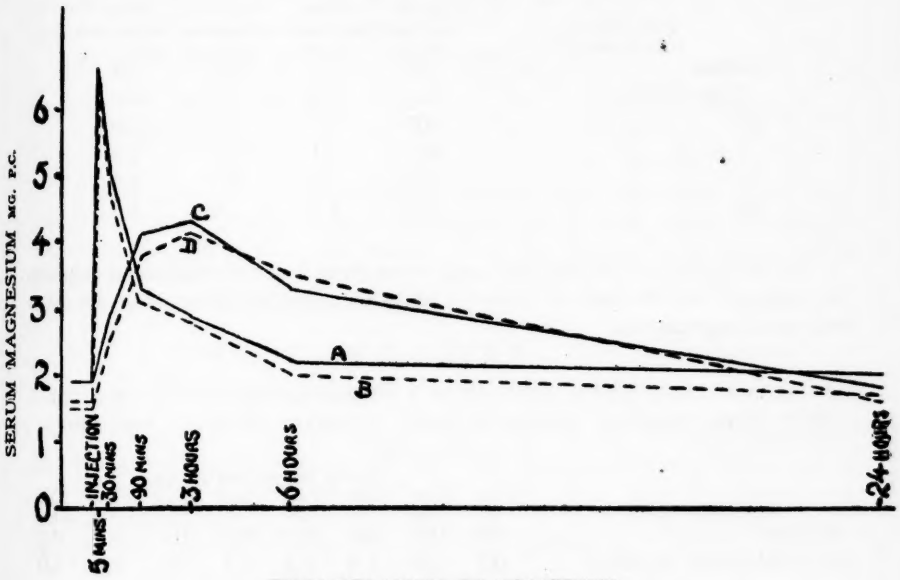

FIG. 7.
Behaviour of serum magnesium after intravenous and subcutaneous injection of magnesium sulphate into cows showing reasonal hypomagnesæmia without clinical symptoms.

Four other cows received daily drenches of 6 ounces of magnesium sulphate for three days, and, as is shown in Table XIII, did not reflect any elevation of serum magnesium level.

TABLE XIII

RESULTS OF THREE DAILY DOSES OF 6 OZ. MAGNESIUM SULPHATE IN COWS WITH SEASONAL HYPOMAGNESÆMIA WITHOUT CLINICAL SYMPTOMS—JANUARY, 1938

Time	Serum Magnesium mg.p.c. Cow W	Cow X	Cow Y	Cow Z
Before drenching	1.7	1.2	2.0	1.5
1 day after 1st drenching	1.8	1.2	2.0	1.5
„ „ 2nd „	1.8	1.0	1.9	1.6
„ „ 3rd „	1.6	1.3	2.1	1.5

In March, 1939, two cows, with lower serum magnesium values of 1.1 and 0.8 mg.p.c., were given 50 g. magnesium sulphate intravenously. The data in Table XIV show that once again the serum magnesium level returned to its initial value and did not steady out in the normal range.

TABLE XIV

RESULTS OF INTRAVENOUS INJECTION OF 50 GRAMS MAGNESIUM SULPHATE IN COWS WITH SEASONAL HYPOMAGNESÆMIA WITHOUT CLINICAL SYMPTOMS—MARCH, 1939

Time Relative To Injection	Cow E Serum Calcium mg.p.c.	Cow E Serum Magnesium mg.p.c.	Cow F Serum Calcium mg.p.c.	Cow F Serum Magnesium mg.p.c.
Before	8.9	1.1	9.8	0.8
5 mins. after	8.8	10.2	9.9	10.0
30 „ „	9.0	6.3	9.7	6.0
3 hours „	9.1	3.1	10.0	2.8
6 „ „	8.9	1.7	9.7	1.3
24 „ „	9.0	1.2	9.8	1.0

In April, 1940, a further eight cows were given 1 ounce magnesium sulphate intravenously and the data in Table XV show the same behaviour as in the other two years' experiments.

TABLE XV

RESULTS OF INTRAVENOUS INJECTION OF 1 OZ. MAGNESIUM SULPHATE IN EIGHT COWS WITH SEASONAL HYPOMAGNESÆMIA WITHOUT CLINICAL SYMPTOMS—APRIL, 1940

Dates and Times	Serum Magnesium mg.p.c. Cow 2	Cow 10	Cow 13	Cow 26	Cow 29	Cow 33	Cow 44	Cow 106
4.4.1940	0.9	0.8	0.9	0.7	0.9	0.5	0.4	0.8
10.4.1940 before injection ...	0.8	0.8	1.0	0.5	1.1	0.5	0.4	1.0
„ 30 mins. after injection	5.4	5.5	5.2	5.2	5.4	4.4	5.0	6.4
11.4.1940	0.9	1.0	1.1	1.0	1.2	0.6	0.7	1.1
2.5.1940	2.0	1.2	1.2	1.2	1.4	0.5	0.4	1.6
6.6.1940	2.0	1.9	1.7	1.5	1.9	0.8	1.2	2.0

Discussion of Results on Swanton Cows

From the results of these experiments it is clear that, in the case of animals with seasonal hypomagnesæmia which is not accompanied by clinical symptoms, the level of serum magnesium is set at a level below that of the commonly accepted normal range of 1.8 to 3.1 mg.p.c. (Allcroft and Green, 1934).

This fact might explain the different behaviour of the serum magnesium which had been observed in certain clinical cases after treatment. Blood samples from four cases submitted to this Laboratory for chemical analysis may be selected to illustrate good response to calcium and/or magnesium injections, in that serum magnesium rapidly returned to normal.

Case W., March, 1935: Cow calved March 18 and showed clinical evidence of lactation tetany. She was injected with 8 ounces 25 per cent. magnesium sulphate intravenously and a similar quantity subcutaneously, and was also given 1 lb. magnesium sulphate by stomach tube.

The chemical data obtained were as follows:—

Date of Sample	mg.p.c. serum Calcium	Magnesium
18 March (before treatment)	4.6	0.3
19 „	6.2	3.6

Case X, January, 1937: Cow had a staggering fit on January 6 and her owner inflated her udder. She calved January 7, and, on clinical diagnosis, was given 16 ounces 20 per cent. calcium borogluconate and 100 ml. 25 per cent. magnesium sulphate subcutaneously. Magnesium sulphate was repeated January 8 and 9 and the cow was normal on the 10th.

The chemical data obtained were as follows:—

Date of Sample	mg.p.c. serum Calcium	Magnesium
7 January	5.2	0.5
9 „	2.9	2.1

Case Y, June, 1937: Cow developed lactation tetany six months after calving and was given 1¼ ounces calcium borogluconate and 1 ounce magnesium sulphate subcutaneously, followed by 1¼ ounces calcium borogluconate, and was reported normal next day. No further sample was obtained for a fortnight.

The chemical data obtained were as follows:—

Date of Sample	mg.p.c. serum Calcium	Magnesium
3 June	4.7	0.8
17 „	10.0	1.8

Case Z, May, 1940: Cow calved May 17 and next day was noted staggering. She was given 3½ ounces calcium borogluconate intravenously and 300 ml. 25 per cent. magnesium sulphate subcutaneously. Four hours later the calcium was repeated subcutaneously. Next day (May 19) she was given ½ lb. magnesium sulphate as a drench. Reported normal when sampled on May 27.

The chemical data obtained were as follows:—

Date of Sample	mg.p.c. serum Calcium	Magnesium
18 May	4.0	0.5
27 „	9.5	2.0

In view of the rapid return of the magnesium to the range 1.8 to 3.2 mg.p.c. serum in these four cases, it would appear likely that the hypomagnesæmia was not of the slowly developing seasonal type, but had developed in a shorter time, maybe even a matter of days, and that the serum magnesium level was not set at the low figure as it was in the Swanton cows.

The question arises as to what constitutes a "normal range" for serum magnesium. Under general dairy husbandry conditions, the normal range found in Weybridge experience was 1.8 to 3.2 mg.p.c. (Allcroft and Green, 1934), and this accords well with the general findings in the literature, but, in the absence of clinical symptoms and in view of the return of serum magnesium to a low level after it was raised by injection of magnesium sulphate, it is hard to believe that the low values shown by the Swanton cows were not "normal" for them at the time. These findings also make it more difficult to assess the true value of a low serum magnesium level in a blood sample from a clinical case, for which no previous data exist, since the rate of preceding fall of the magnesium cannot be gauged from one sample.

Summary

1. The behaviour of calcium and magnesium in the serum of ruminants has been studied following certain experimental procedures.

2. Oral administration of 6 ounces magnesium sulphate daily for several

days had no effect on serum magnesium level of the adult bovine.

3. "Prolan" injections did not alter the level of serum magnesium in rabbits, goats or heifers.

4. Calcium and magnesium injected intravenously caused an immediate rise of the element injected, whether they were administered singly or together, but the excess in the serum disappeared rapidly.

5. Subcutaneous injection resulted in a slower rise, a lesser degree of elevation and a longer period of elevated level of either mineral.

6. In cows with seasonal hypomagnesæmia without clinical symptoms the serum magnesium, after elevation by injection of magnesium sulphate, returned to the pre-injection level and not to the "normal" range of 1.8-3.2 mg.p.c., as it did in many cases of clinical hypomagnesæmia, suggesting that the low seasonal value was normal for the animals at the time.

7. The anæsthetic level of serum magnesium in the ruminant is about 14 mg.p.c. and the lethal level about 20 mg.p.c.

8. The different routes of injection are discussed in relation to field therapeutic treatment of metabolic disorders.

Acknowledgments

To Dr. H. H. Green, under whose direction the work was carried out and whose name appears as senior author in earlier papers of the series; to Dr. Ruth Allcroft for her collaboration; to Mr. F. J. Salt for technical assistance; and to Mr. Edward Rice for permission to carry out experiments at Swanton Farm.

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XUM

CONGENITAL ENLARGEMENT OF THE ULNAR HEAD OF THE DEEP DIGITAL FLEXOR (Flexor Perforans) IN THE HORSE

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An interesting case of growth irregularity in a single limb muscle was presented for examination.†

Subject

Fifteen-month-old thoroughbred filly, twin to another filly. The dam had been barren for five years prior to holding service with these twins and has since aborted twin foals. The twin died at four months of age from strongylosis.

History

The filly was normal until six weeks before she was killed. The symptoms observed were a disinclination to move accompanied by weakness of the near fore with knuckling of the fetlock and carpal joints, apparently due to contraction of the flexor tendons. Palpation of the limbs revealed no anatomical abnormality. Slight improvement was noticed after 14 days, but the symptoms soon returned and remained present until the end. The relapse coincided with the appearance of similar symptoms in the off fore which became progressively worse and necessitated destruction of the animal.

The stance adopted in the box was protraction of both fore limbs. At the walk the foot was brought to the ground normally but could bear no weight and simply knuckled at the fetlock. At times the toe was dragged along the ground. Towards the end the animal could not walk. She never actually fell.

The off fore leg was sectioned at the elbow immediately after death. External examination revealed no anatomical abnormality. There was marked wear on the lateral quarter of the toe which gave a slope to the ground border of the wall, and, as all the joints were in the normal linear plane, the limb must have been carried in adduction.

Anatomical Findings

Dissection was commenced at the coronet. Evidence was found of synovitis on the anterior aspect of the synovial membranes of the fetlock and carpal joints, attributable to the effects of knuckling, and of slight reorientation of tendons and ligaments in accordance with the slope of the foot, but all other structures were macroscopically normal. Particular attention was paid to the vestigal structures in the limb of the horse—the interossei and lumbricales tendons—and although the lateral lumbrical was lacking and the lateral interosseous poorly developed, no particular significance was attached to this as their form is often irregular and they were not associated with any abnormality of tissue. Not until the elbow was reached was evidence presented of any gross irregularity to which the symptoms could be attributed. The muscular belly of the ulnar head of the deep flexor,

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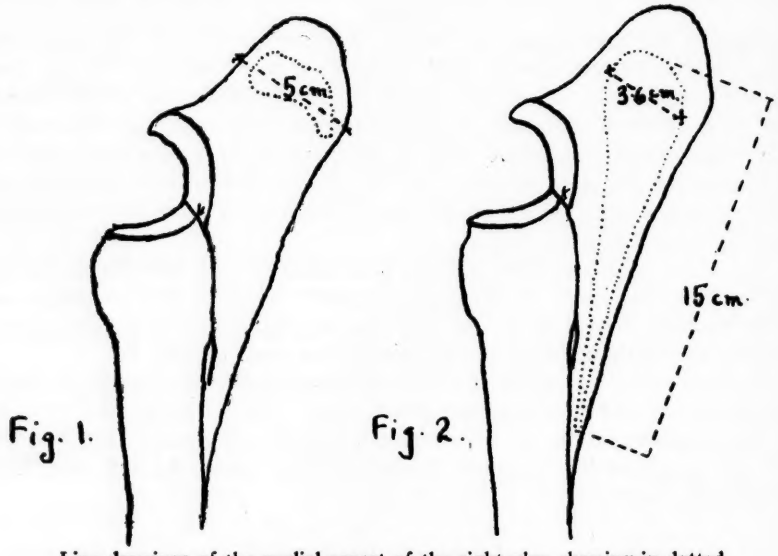
† The specimen and history of the case was supplied by Mr. E. S. Paterson, M.R.C.V.S., of Windsor.

which arises from the medial aspect of the olecranon process of the ulna immediately below the summit and joins with the main tendon near the carpus, had a greatly increased area of origin and was enlarged up to eight times normal size.

The belly took origin from almost all of the available space on the medial aspect of the ulna (see figures) and measured 15 cm. in length, 3.6 cm. at greatest width (immediately below the summit), from whence the width of origin gradually narrowed to a point level with the superficial junction of muscle and tendon. For comparison of these measurements with the normal limb, the width of the olecranon below the summit measured 5 cm. In spite of this extensive origin, there was no interference with the attachment of adjacent muscles, i.e., triceps, anconeus, flexor carpi ulnaris. Although quite thin proximally, the belly had attained a thickness of 3.2 cm. at the level of the sigmoid notch, to again reduce in thickness as it passed down the ulna.



Line drawings of the medial aspect of the right ulna showing in dotted outline the area of origin of the ulnar head of the deep digital flexor: Fig. 1 in the normal leg, Fig. 2 in the case under review.

In the normal limb, the fleshy portion of this muscle is replaced by tendon at about the middle of the radius, but if dissected the tendon will be found to extend for a distance within the muscular sheath and tendinous fibres are found almost to the origin. In this specimen the arrangement of tendon fibres was the same in principle and the course, size and attachments of the tendon were normal, although the level of origin of the tendon proper within the sheath was more distal. Thus more of the tendon was enclosed by muscle fibres and, at the distal end of the ulna, the lowest fibres of origin of the muscle coincided with the appearance of the independent tendon. No histological preparations were made, but the muscle fibres had every appearance of normality on macroscopic examination.

Discussion

The near fore leg was not dissected, but from the similarity of the symptoms exhibited it is more than probable that similar findings would have been found. However that may be, it is remarkable that in the off fore leg abnormality of growth was present in a single unit. No evidence can be found in the literature of a genetic factor responsible for such a growth, although it is not uncommon to discover atrophy of single muscle units or multiplication of tendons and bones. The congenital nature of the abnormality, however, seems quite definite and the irregular breeding habits of the dam may have been a contributory factor.

Again, no physiological evidence can be found to demonstrate that in the complicated pattern of muscular activity increase in size of one unit of movement will greatly affect the resultant movement; circumstantial evidence presented in this case, however, suggests the possibility that knuckling of the fetlock and carpal joints was due to increased tension in the deep flexor consequent upon an increase in size and area of origin of the muscular belly of the ulnar head.

Why the symptoms did not appear until the animal was one year old is less easy of explanation, but once in evidence their effect was pronounced and they became progressively worse. One can only assume, therefore, that rapid growth changes began in the congenitally abnormal tissue immediately before the onset of symptoms.

The posture and gait of the animal was typical of a case of contracted flexors at least in the beginning; but it is not surprising palpation of the limb was negative as the site of the trouble was atypical, and had attention been drawn to the elbow it would have been difficult to locate the enlarged muscle on account of its close association with surrounding structures.

Summary

A case of congenital abnormality of the ulnar head of the deep flexor muscle characterised by increase in size and area of origin of the muscular belly is described. The animal exhibited symptoms of knuckling of the fetlock and carpal joints and it is suggested the symptoms were due to increased tension in the deep flexor muscle consequent upon this abnormal growth.

CLINICAL ARTICLE

TWO CASES OF PERIARTERITIS NODOSA IN THE OX

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DESPITE the rarity of its occurrence, Periarteritis Nodosa in Man has now been fairly thoroughly documented. Since and including the first accurate description of the disease by Kussmaul and Maier (1866), Joest (1922) and Harris and Friedrichs (1922) have independently assessed the number of references as 52, Arkin (1930) put the number of recorded cases from 1866 to 1930 at 150, while Middleton and McCarter (1935) put the number at approximately 200 up to 1935.

How many cases have been recorded since we cannot say, but since 1866 there has been sufficient material to enable Arkin (1930), for one, to work out a possible pathogenesis of the disease and for many other workers to investigate its ætiology. Harris and Friedrichs (1922), having read some reported instances in the lower mammals, suggested that these formed a reservoir of infection from which there might be contagion to human beings. But if one could judge by the paucity of published case records in the lower mammals, the disease would seem to be of even rarer occurrence in them than in man. The following are all that we could trace :—

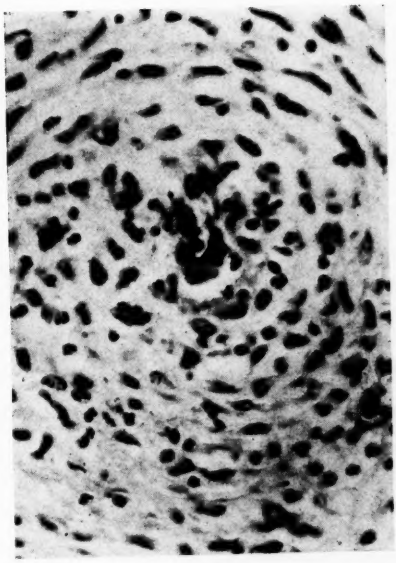
Lüpke (1906).—Lüpke is accredited with the first description of the disease in animals other than man. In a herd of 100 Axis deer, 49 animals died between 1890 and the beginning of 1897. He described the situation of the lesions observed *post mortem* in detail, their macroscopic appearance in more general terms, but gave no histological description. Various clinical courses were differentiated, but only in the less severe but more prolonged cases, marked by anæmia and marasmus, did he feel entitled to describe the vascular lesions as Periarteritis Nodosa. Thus Periarteritis Nodosa was for him not a clinical entity *per se* but one manifestation of another, more variable, more generalised condition which he designated "Axiskrankheit." The course of events throughout his observation of the herd led him to suspect a contagious disease, but the cocci which he recovered from the blood and vascular lesions of affected animals were not pathogenic for laboratory animals and he did not have the opportunity of inoculating young, healthy deer. Jaeger (1909) dealt with the histology of some material sent him by Lüpke from an Axis deer and tried to work out the sequence of the vascular changes. His histological description of the lesions—there are no illustrations—shows them to have many points in common with Periarteritis Nodosa as we now recognise it. He thought the sequence of events to begin with a granulomatous disorder of the vascular adventitia—with "round cell" infiltration—leading to invasion of the media, rupture of the elastic interna and obliteration of the lumen by fibroblasts succeeded by scar tissue. He saw no aneurysms and reported no nodule formation.

Guldner (1915).—A four-weeks-old calf with nodules in the masseter muscles and tongue. The condition was thought at first to be cysticercosis, but further nodules were found *post mortem* in the heart and skeletal muscles, nodules which, on microscopical examination, were found to be lesions of Periarteritis Nodosa.

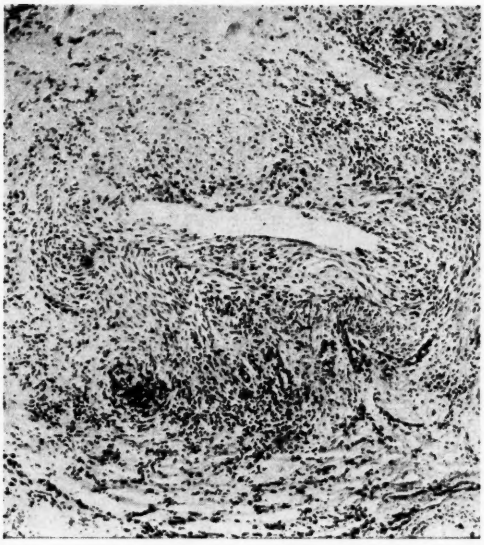
Joest and Harzer (1921).—(1) A two-year-old slaughtered pig with no clinical history. The only affected animal in the herd; only the kidneys were involved and the changes were nodosal in form. (2) A one-year-old slaughtered pig which had been paralysed just prior to slaughter. Kidneys, spleen, stomach, mesentery, ovaries, fallopian tubes, mesovarium, mesosalpynx and uterus were all affected, the vessels being thickened and thrombosed, the lesions nodosal or continuous.

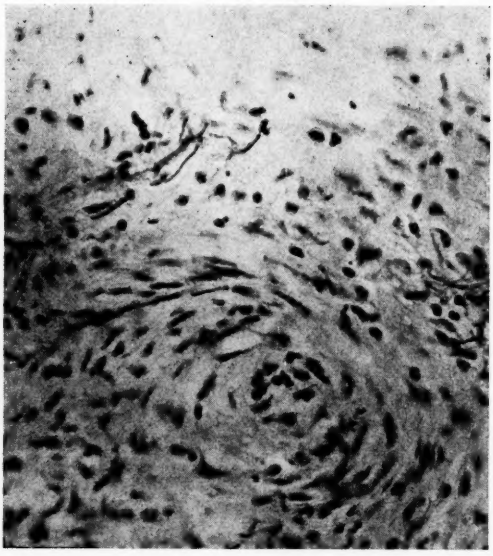
Balo (1924).—A four-year-old fox terrier dog exhibiting clinical symptoms of gastro-enteritis and nephritis. *Post mortem* examination revealed acute gastritis, parenchymatous nephritis and Periarteritis Nodosa affecting only the coronary arteries.

Hoogland (1925).—(1) A slaughtered pig clinically normal prior to slaughter and normal at autopsy but for Periarteritis Nodosa of both kidneys. (2) A



TWO CASES OF PERIARTERITIS NODOSA IN THE OX
See pages 179-184





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slaughtered ox normal in every respect but for the typical lesions in a portion of superficial skeletal muscle. (3) One extensive case in a slaughtered ox, skeletal muscles, kidneys, heart, coronary fat and lung parenchyma being affected, although the animal was well nourished and showed no clinical symptoms.

Montroni (1934).—A three-year-old cat without clinical history. Lesions of Periarteritis Nodosa were found in the intercostol, coronary, mediastinal, gastric and mesenteric arteries and in the arteries of the kidneys. A large hæmatoma in the mediastinum was the apparent cause of death and probably arose from a ruptured aneurysm.

Schoon (1934), who reported the condition in a slaughtered cow.

Craig and Davies (1941).—These authors, discussing Periarteritis Nodosa in cattle, said that they had two specimens in their collection and had seen a number of others. They then recorded one case of the disease diagnosed *post mortem*, lesions being seen in the general musculature, myocardium, sub-epicardial fat and mammary gland, the aorta and the larger blood-vessels being normal. Their previous observations included lesions in the spleen, renal cortex, liver, lungs, tongue, diaphragm and in the muscles of the back and thighs.

Hansen and Jensen (1942) observed the presence of lesions in the heart, liver and kidneys of a pig.

Pallaske (1943).—A 13-months-old pig. The affected heart and kidneys were submitted for examination with the information that the condition was widespread throughout the carcase.

Wickware (1944) considered the condition to be very rare, having encountered it only three times in 35 years. He then described two of these instances: (1) A two-year-old heifer in which the myocardium and general musculature were involved. (2) A four-year-old cow in which the heart, udder, lungs and skeletal muscles were all affected.

Kilchsperger and Stünzi (1946).—These authors encountered the condition in 23 out of 1,068 carcasses or morbid specimens from pigs, sent to them from east and central Switzerland. In all the hearts were affected, in 21 the kidneys, in three the lungs, but in only one were lesions found in the skeletal muscles.

Other references are: Stebler (1930), Redlich (1935), Schmidt (1939), Swoboda (1940), and Bisbocci (1941).

Our standard textbooks of meat inspection and veterinary pathology barely mention the disease: Joest's contributors, Ackerknecht and Krause (1929) and Nieberle and Cohrs (1931) give a few references which have already been discussed above; Ostertag (1934) cites Lüpke and mentions the condition in a sheep, but as he gives no references this could not be traced; Hutyra, Marek and Manninger (1938) put the records as follows: four cases in the pig, seven in cattle, one in the dog and one in the antelope—but give no references.

Specimens from two cases of Periarteritis Nodosa were received from Mr. T. Johnston and from Captain E. J. Burndred, and the ensuing reports are based on their observations on the carcasses and our detailed examination of the pieces of tissue received. These were fixed in 10 per cent. formol saline and embedded in paraffin wax, sections being stained by Ehrlich's hæmatoxylin and eosin, Weigert's iron hæmatoxylin and van Gieson's stain, azan stain, and Hart's stain for elastic connective tissue fibres counter-stained with neutral red.

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Case I.—A slaughtered Hereford steer in poor condition. "The carcase had a reddish, congested appearance due to the presence of numerous small, thickened blood-vessels in the subcutaneous tissues. The condition was present in the muscles, especially in the pectoral region; there was also evidence of it in the kidneys and heart." Prior to slaughter, the steer was seen to have a slight swelling of the hind fetlocks, but there was no lameness.

The tissues sent comprised strips of the pectoral and gluteal muscles with their covering of fascia and subcutaneous connective tissue, portions of kidney and a small piece of myocardium. These were unpreserved and had taken a few days to reach the laboratory, but treatment with Jores I and coal gas made possible fairly accurate macroscopical examination. The vessels of the muscle fascia were thickened and dark red, standing out clearly from the surrounding connective tissue, their walls thickened on transverse section, their lumena patent. The smaller vessels penetrating the interfascicular tissue of the muscle were likewise thickened and clearly visible, though white in colour and not always patent. The myocardium was not pervaded by thickened vessels in the same way, but the coronary vessels (in the strip of myocardium received) were quite obviously affected. The surface of the kidney looked quite normal, its capsule stripping easily. On section, the renal parenchyma was mainly normal too, though one lobule had several grossly affected vessels showing in transverse section in the cortex; but many of the vessels in the interstitial tissue, particularly the arcuate vessels, were severely altered, prominent and thickened.

Case II.—A slaughtered heifer which had been totally condemned at meat inspection. All the offals were œdematous, the liver normal in colour and consistence but for two abscesses; no gross lesions of tuberculosis were observed; the outside of the dressed carcase, including the head and limbs, bore numerous papules. On closer examination, the entire carcase was seen to be studded with what appeared to be small cysts " from a millet seed to a lentil, or even a pea, in size."

We received a small, unpreserved strip of affected beef some three or four days after the heifer had been killed. The fat had improperly set while the muscle tissue was very pale and studded with discreet, translucent nodules equal in size to the head of a large pin, sometimes in groups of two and three.

Histology

Case I.—The changes observed in the vessels were, on the whole, typical of the later stage of Periarteritis Nodosa (as described by Arkin, 1930) with the formation of collagenous fibrous tissue in and around the walls of the injured vessels. This granulation tissue had already become avascular, but proliferating fibroblasts had not yet given way to acellular scar tissue. No mention had been made in the *post mortem* report of infarcts nor had we seen any, or other ischæmic lesions in the tissues received. Histological examination supported this. Some small vessels were completely obliterated by collagenous fibrous tissue which reached out into the adventitia, greatly adding to the thickness of that coat, but most of the vessels were patent though their elastic intima had been stretched and weakened, sometimes apparently ruptured, and the endothelium had greatly proliferated. This was shown most clearly in the largest vessels, the elastic intima appearing as a thin, more or less complete, coat surrounding the proliferated

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endothelium. All these changes were least intense in the largest vessels examined, as too were the alterations in the media. In the most drastically affected vessels, the muscular media was completely replaced by massive formations of scar tissue which, along with the collagen fibres of the adventitia, formed (microscopically) huge masses of fibrous tissue around the vessels. Some of the lesions had been infiltrated at their periphery by eosinophil leukocytes. We noticed, too, a brown granular pigment, probably hæmosiderin, in the obliterated vasa vasorum of a severely affected large vessel.

In the previous paragraph we have consistently referred to "vessels." We saw many normal veins and lymphatics in the sections examined, but no normal arteries or arterioles. Apparently this vascular disease had affected only the arterial system.

Case II.—This did not present the same variety of changes as Case I. Most of the arteries were obliterated, the remaining few almost so. There was some, not very great, infiltration by eosinophils. Groups of affected arteries had coalesced into large masses of collagenous fibrous tissue in which few elastic fibres could be seen.

Discussion

Periarteritis Nodosa, as Boyd (1943) observes, is a misleading name, since the vascular changes constitute a *pan*arteritis, not a *peri*arteritis, and the condition is by no means always nodosal. This certainly agrees with our findings. In one case the changes were continuous along the vessels, in the other there was considerable nodule formation; in both there was involvement of the entire thickness of the arterial wall and surrounding adventitious tissue. But though the name is misleading, it is used in this article because of its general acceptance.

The presence in some lesions of eosinophil polymorphonuclear leukocytes we do not regard as sufficient evidence for the suggestion, made by Craig and Davies (1941), that the changes are caused by helminths. No metazoan parasites or their remains were observed in the lesions of the morbid specimens received. Unfortunately the latter were not fresh enough for animal inoculation experiments, for Haun (1920) and Harris and Friedrichs (1922) inclined to the theory of a virus origin; though in saying this we do not overlook the great mass of experimental work—mainly American—which indicates that the vascular changes may be due to an anaphylactic type of hypersensitivity.

Perhaps the most important feature of Periarteritis Nodosa in man is its polysymptomatic character, febrile in the early stages, the symptoms ultimately varying according to the organs rendered ischæmic. In none of the recorded instances in the lower animals was the disease diagnosed during life, while definite symptoms were observed in only a few of them. This may be due to various factors: perhaps symptoms were present but not noticed; perhaps a febrile complaint or vague malaise was attributed to some other cause and not associated with the arteritic lesions discovered at autopsy some months later; perhaps, as in one of our cases, chronic panarteritis did not result in occlusion of the arteries, so that blood passed through sufficient to prevent functional changes in vital organs. We can see little possibility of diagnosing the disease in the living animal—which

is tantamount to saying that it remains of interest mainly to the meat inspector and the research worker.

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ABSTRACTS FROM CURRENT LITERATURE

PICA IN CATTLE: REPORT ON A MANURING TRIAL WITH COPPER-SLAG FLOUR

By H. J. GERRITSEN

Tijdschrift voor Diergeneeskunde, 71, 18, 709-720, *September,* 1946.

A REPORT on a manuring experiment with copper-slag flour to combat pica in cattle in consequence of a disturbed copper economy on river-clay soil at Bergharen.

Although customary method for examination for the presence of copper in soil showed no deficiency of copper, the grass and cattle which did show signs of copper deficiency reacted most favourably on manuring with copper-slag flour.

A FORM OF TETANY IN CALVES

By W. V. D. BERG

Tijdschrift voor Diergeneeskunde, 71, 21, 833-841, *November*, 1946.

A FORM of tetany in calves is described with the usual symptoms but showing a characteristic "dissecting" image of the muscles. Blindness occurring some considerable time before the convulsions was also a marked symptom.

Vitamin A deficiency could most probably be excluded. It was thought that a shortage of one of the component parts of milk fat rather than too much albumin was a probable exciting factor.

RESEARCH INTO THE SPEED OF DEVELOPMENT OF EGGS AND LARVÆ OF HORSE STRONGYLES

By P. WAGENAAR HUMMELNICK

Tijdschrift voor Diergeneeskunde, 71, 18, 842-852, *November*, 1946.

THE quickest development of strongylid-eggs in horse fæces occurs at about 35 deg. C.; at this temperature the first larvæ stage may be reached in 10 hours. Higher temperatures are harmful; at 40 deg. C. the development of the embryo has stopped. Development is delayed when temperature is reduced. At 18 deg. C. the first larvæ stage will be reached in about 1½ days; at 8 deg. C. only after 12 days. Probably at 3 deg. C. all development has ceased.

The average time necessary for reaching the tadpole, vermiform, first larvæ or third larvæ stage is in proportion of about 10 : 15 : 27 : 100.

The times necessary for the development of the morula plus gastrula stage, tadpole, vermiform and first plus second larvæ stage are as 20 : 10 : 20 : 150. Calculating the relative velocity at different temperatures for these stages separately, we observe that the curves which can be constructed show a striking similarity. However, the rate of development in the larvæ stage, compared with that of the embryonial stage seems to be somewhat higher between 10 deg. and 15 deg. C. and between 25 deg. and 30 deg. C., and has already reached its optimum at 30 deg. C.

The temperature coefficient (Q_{10}) of the embryonial development is high about 20 to 2 between 10 deg. and 15 deg. C. and about 1½ between 30 deg. and 35 deg. C.; the (Q_{10}) of the larvæ development, on the contrary, shows values from about 4 to 2 between 10 deg. and 25 deg. C. and about 1 between 30 deg. and 35 deg. C.

RELATIVE TOXICITY TO SWINE OF LEAD ARSENATE SPRAY RESIDUE, LEAD ARSENATE, LEAD ACETATE AND ARSENIC TRIOXIDE

By KERMIT GROVES, ERNEST C. McCULLOCK, J. L. St. JOHN

J. Agric. Res., 73 (5), 159-166, 1946.

THE routine use of large amounts of lead arsenate sprays in orchards has led to the view that such sprays are only moderately toxic. There has been some clinical support for this view, and the present communication deals with a full

investigation into the amounts likely to be fed by feeding sprayed apples to swine and the amounts actually absorbed. Six swine were used. Pig 1 was fed with maximum amount of spray residue it would receive if it consumed *ad lib* quantities of sprayed apple peelings, calices and stems. Pig 2 an equal amount of lead arsenate powder. Pig 3 an equivalent amount of lead as lead acetate. Pig 4 an equivalent amount of arsenic as trioxide. Pig 5 one-quarter as much spray residue as Pig 1. Pig 6 received no lead or arsenic and served as a control. All pigs received mixed grain, tankage, salts, etc., as required. The first series of experiments (weight gains) lasted for approximately 3½ months, and the second series on all but Pig 3—which died somewhat unaccountably—for about 6 months. All pigs showed increases in weight comparable with the control and none any abnormalities, although in one case one pig consumed spray residue equivalent to nearly 4 oz. lead arsenate from nearly a ton of apples, considerably more than a pig feeding on normally sprayed apples would receive. Analysis of the organs of Pigs 1 and 2 showed that of the edible portions only the livers contained more lead than the authorised limit of 7.14 p.p.m. as laid down by the Federal Security Agency (Food and Drug Administration), and none of the organs contained more than the authorised limit of 3.57 p.p.m. arsenic trioxide.

D.G.H.

THE PERCUTANEOUS ABSORPTION OF ARSENIC BY SHEEP DIPPED IN ARSENICAL SOLUTIONS

By J. L. HILL

J. Council J.C. Scien. Ind. Res., 19 (3), 251-255, 1946.

SIX adult sheep weighing 68-87 lb. and shorn 60-65 days previously, absorbed 63-88 mg. arsenic (as trioxide) after being dipped in a normal solution containing 0.2 per cent. arsenic as trioxide. None of the sheep showed any serious effects, and even one 12-month weaner in poor condition with various shear cuts did not absorb enough arsenic to account directly for its death, which was undoubtedly hastened by bacterial infection consequent upon severe arsenical inflammation of an axillary shear wound. The author rightly draws attention to the danger in assuming that relatively large quantities of arsenic found in the rumens of sheep suspected of arsenical poisoning are due necessarily to the animals having swallowed quantities of the dip, since analysis of sheep's saliva showed that its arsenical content was up to thirtyfold that of blood after a normal dip where every precaution was taken to prevent liquid actually entering the mouth.

D.G.H.

TEMPERATURE MEASUREMENTS IN THE HUMAN AND BOVINE FEMALE APPLIED TO REPRODUCTIVE PHYSIOLOGY*

DURING the menstrual cycle the body temperature at rest shows a diphasic fluctuation: in the premenstrual (secretory) phase, lasting 12 ± 3 days in all

women, the temperature rises above the mean; in the postmenstrual (proliferative) phase, lasting for the remainder of the menstrual cycle, the temperature falls below the mean.

The œstrus cycle of the cow is also accompanied by a diphasic fluctuation of the body temperature. Here the phase of low temperature (6 ± 4 days) begins with the brief procœstrus and ends at the commencement of metœstrus. The phase of high temperature (15 ± 3 days) coincides with the full development of metœstrus. In spite of distinct signs of heat, however, the typical temperature curve was found only in some 50 per cent. of the animals examined.

In pregnant cows the temperature is lowered in the first 4 months, followed by an approach to normal and a second fall towards term. There may be a marked drop 1 to 2 days before parturition, prognosticating the onset of delivery. In the single case of a woman cited the temperature showed an inverse course: a sharp rise at the beginning, a fall to normal in the middle, and a renewed high rise towards the end of pregnancy, terminating in a steep drop after parturition.

H.R.

* R. and U. Vollmann: "Temperature Measurements in the Human and Bovine Female Applied to Reproductive Physiology." *Schweizer Archiv. für Tierheilkunde*, November and December, 1942, lxxxiv, Bd., II, Heft.

FACTORS INFLUENCING DISTRIBUTION OF ARSENIC OVER FLEECE OF SHEEP AFTER IMMERSION IN ARSENICAL SOLUTIONS

By J. L. HILL

J. Council J.C. Scien. Ind. Res., 19 (3), 245-250, 1946.

THE popularity of arsenic as an insecticide in controlling the body louse of the sheep (Bovicola ovis) has stimulated further researches into the means of increasing the efficacy of such solutions. This communication deals primarily with the effects of suint (potassium salts of the lower fatty acids) and proprietary wetting agents on the retention of arsenic in wool, and a comparison of the results of Hobson's experiments on "open fleeced" Welsh Mountain sheep with those obtained after conducting similar experiments under Australian conditions on "close fleeced" Merino sheep. Detailed experiments indicated that arsenic distribution was very irregular and no explanations of this are proposed. Furthermore, neither the accumulation of suint nor the presence of wetting agents appeared to have any effect on the amount of arsenic left in the wool. The latter result is contrary to that of Hobson. The only factor found to influence arsenic retention was staple length, and where wool was long, e.g., on the belly, good drainage occurred and therefore less arsenic was retained, whereas retention was much better with closer-cropped sheep.

D.G.H.

NEWS

THE USE OF HISTAMINE IN THE TREATMENT OF SEASICKNESS*

(Whilst not of immediate veterinary interest, this note may be of interest to veterinary surgeons who are unfortunate victims of this distressing malady.—*Ed.*)

Because of the reported successful results obtained in treating some selected cases of aural vertigo with histamine and because of the similarity existing between this syndrome and the symptom complex of seasickness, a medical officer studied the effects of histamine in the treatment of seasickness.

Fifty-four men among Army personnel travelling aboard an A.K.A. en route from San Francisco to the Marshall Islands were the subjects for this study. The men had several things in common. It was their first sea voyage; all became ill after about twelve hours out of port; all had giddiness, nausea, and vomiting in varying degree; and all were ill enough to refuse food and to justify confinement to bed.

In order to determine whether or not there existed in the patients any unusual degree of sensitivity to histamine, 0.1 mg. of the drug was injected intradermally in each. One-half hour later the reactions were graded and recorded and the patients grouped as follows:

Group No.		*Graded as*	*No of patients*
1	No wheal, no erythema	Neg.	3
2	Wheal with less than 1 cm. erythema ...	1 plus	5
3	Wheal with erythema 1-3 cm.	2 plus	16
4	Wheal with more than 3 cm. of erythema	3 plus	30

Fifteen of the patients were selected as controls (2 from group 1, 4 from group 2, 8 from group 3, and 1 from group 4).

The 39 men selected for treatment received three doses of 0.5 mg. histamine administered intramuscularly at intervals of three hours. No untoward reactions were encountered. After the second injection of 0.5 mg. histamine, 20 patients experienced relief and were able to eat food and walk about with no sensations of nausea or giddiness.

The following morning, after all three injections had been received, 37 of the patients were entirely symptom-free. Two felt only moderately better. All the controls were still sick and remained so for three more days despite scopolamine, aspirin, and other drugs.

In view of the encouraging results achieved in this small series and the absence of any other efficacious remedy, more studies in the treatment of seasickness with histamine seem advisable.

* U.S.A. Medical Services Bulletin.

XUM

TUBERCULIN TESTING: ADOPTION OF THE SINGLE INTRADERMAL TEST

EXPERIMENTS aimed at improving the efficiency of the tuberculin test have been in progress for several years. Among other matters investigated has been the question of whether a single intradermal tuberculin test would give results as accurate as those obtained by the double intradermal test. The latter test has been used in Great Britain for many years but has not found favour in any other country.

The most recent experiment, covering nearly 10,000 cattle, was completed in 1946, and it has shown a close comparison between the results yielded by the two tests. In attested herds and "T.T." herds it was the single test which gave the more accurate result in the few discrepancies that occurred. The Agricultural Research Council have considered the results of the experiment and are satisfied that on the scientific evidence before them the single test proved as effective as the double.

Whereas the double intradermal test requires two visits for injections and a third visit for the final observation, the single test requires only two visits, one for injections and one for observation, and thus saves labour both for the farmer and the veterinary surgeon without loss of accuracy. Accordingly, it has been decided that as from a date to be announced shortly, the single intradermal test will be used for all official tests of attested herds and T.T. herds.

March 28, 1947.
1947 Tech. No. 7.

REVIEW

Thoughts on Feeding. By LIONEL JAMES PICTON, O.B.E. Price: 12s. 6d. net. London: Faber & Faber, Ltd.

DR. PICTON was one of the members of the County Palatine of Chester Local Medical and Panel Committee who drew up the well-known Medical Testament which focused attention on sound nutrition as being the key to good health. All the members who signed this declaration of their faith were enthusiasts urged on by deep conviction, and not the least of these was Dr. Picton. Sir Albert Howard and his followers also subscribe to this faith, and it is through his efforts that the health of the soil has become such a feature in ensuring good health in humans and in animals. Briefly, their argument is this: that the well-being of man depends upon his food, animal and vegetable, and the latter in turn depends upon the healthy fertility of the soil. The soil must be kept in good health and to do this nature's methods are best. Nature refreshes and stimulates the soil by making use of decayed organic matter and we can follow her lead by employing scientifically prepared compost.

Dr. Picton has gathered together within the pages of his book all the relevant information on this most intriguing subject.

His theories are backed by historical data and by experimental and practical research work of modern times sufficient to influence even the most sceptical.

The reader will not lay this book aside lightly: he will read on and ponder, for if the arguments are right—and indeed they are certainly most convincing—is it not possible that in these pages we have a testament which can bestow untold blessings on mankind?

Veterinary surgeons and agriculturists will find the book of particular interest, and we commend it to their attention.

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